

REMARKS/ARGUMENTS

Claims 1-12, 14-18 and 20-22 are pending in the captioned application.

Claims 11, 12 and 14-18 are withdrawn. Claims 1-10 and 20-22 are rejected.

Applicants hereby cancel the non-elected claims 11, 12 and 14-18. Applicants have also amended claim 1 and cancelled claims 20 and 21. Applicants respectfully request reconsideration and allowance of claims 1-10 and 22.

The declaration was objected to by the Examiner. The Examiner states that alterations have been made to the declaration where it was not initialed and/or not dated. In response, Applicants respectfully request reconsideration. Applicants submit that the only change to the declaration was an update of the post office address for Cecilia Kepka. This change was made by the inventor when the declaration was signed; further, the change was made adjacent to the inventor's signature and date. In addition, Applicants submit that this change is a minor deficiency and respectfully request waiver as per MPEP 602.3. As such, Applicants respectfully request reconsideration and withdrawal of this objection.

Claims 1-10 and 20-22 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. Applicants respectfully disagree.

Claim 1 has been rejected as the limitation "the top phase" in step (e) lacks sufficient antecedent basis. In response, Applicants submit that claim 1 has been amended obviating the rejection.

Claims 20 and 21 stand rejected for they are use claims, both under 35 U.S.C. §112 and 35 U.S.C. §101. In response, Applicants have cancelled these claims, rendering the rejection moot.

Claims 1-5, 8-10 and 20-22 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Ageland et al. (US 6,107,467) in view of Ohlsson et al. (Nucleic Acids Research, 5(2):583-90). Applicants respectfully disagree.

Applicants first submit that claim 1 has been amended to better define the claimed invention. In particular, step (c) has been amended to specify that plasmid DNA partitions to a top phase while RNA partitions to a lower phase (page 18, lines 13-15 and Figure 2). Steps (b), (d) and (e) are also amended for consistency of the claim language.

Applicants submit that Ageland et al. relates to the separation of hydrophobic proteins (i.e., ApoA or ApoE) from contaminants including nucleic acids, such as genomic DNA, RNA, as well as plasmid DNA, using aqueous two-phase separation followed by temperature-induced phase separation. Although Ageland et al. discusses in the background section that aqueous two-phase separation has been used broadly (including for the purification of nucleic acids), the Ageland et al. system is used specifically for the separation and purification of hydrophobic proteins.

Ohlsson et al. uses a PEG/dextran system to separate double stranded plasmid DNA from denatured chromosomal DNA and RNA by a method involving denaturation of a mixture of plasmid and chromosomal DNA. According to Ohlsson et al., after denaturation, a two-phase partitioning system can be applied to purify

duplex plasmid DNA from single stranded DNA and bacterial RNA, which method utilizes the fact that the plasmid will re-anneal quicker than the other nucleic acids and hence double-stranded DNA is separated from the other nucleic acids which have still not re-annealed. Ohlsson et al. teaches that these different re-annealing rates are key to allow separation of plasmid DNA from other double stranded nucleic acids. There is nothing in Ohlsson et al. that suggests that plasmid DNA can be isolated in a two phase partitioning system without a preceding denaturation step.

Applicants submit that it is Applicants' position that the references, whether individually or combined, do not teach claim 1 of the instant application. In particular, none of them teaches the use of aqueous two-phase separation followed by temperature-induced phase separation for separating plasmid from other nucleic acids such as RNA.

Applicants submit that Ageland et al. shows that their system removes nucleic acids from the final purified ApoE product (i.e., Table IV, which shows an over 1000 times reduction in plasmid DNA level). However, as the purpose of Ageland et al. is to obtain a purified hydrophobic protein, the skilled person would understand that when Ageland et al. refers to "nucleic acids", it embraces DNA including plasmid DNA as well as RNA, and that there would be no reason or benefit for Ageland et al. to separate one nucleic acid (plasmid DNA) from other nucleic acids (such as chromosomal DNA etc).

The Examiner argues that as the apolipoprotein has been produced recombinantly, there will be plasmid present which will be partitioned. However, as

explained above, even if plasmid DNA would be present such plasmid would in the Ageland et al. method partition together with other nucleic acids. It is noted that Table IV of Ageland et al. reports the removal of “nucleic acids” after the step of thermal separation (not after the aqueous two-phase separation)

Applicants submit that as discussed above, Ageland et al. does not teach the separation of plasmid DNA from RNA, while Ohlsson et al. teaches aqueous two-phase separation, which needs to be preceded by a denaturation step, to separate plasmid DNA from chromosomal DNA and bacterial RNA. For these reasons Applicants submit that combination of Ageland et al. with that of Ohlsson et al. is improper. The combination does not teach or suggest that the Ohlsson et al. denaturation preceding aqueous two-phase separation could be replaced by temperature-induced phase separation subsequent to the aqueous two-phase separation. Even if the references are combined, they would not render obvious the claimed invention.

Claims 6 and 7 are also rejected under 35 U.S.C. §103(a) as being unpatentable over Ageland et al. (US 6,107,467) in view of Ohlsson et al. (Nucleic Acids Research, 5(2):583-90). Applicants respectfully disagree. Applicants submit that as discussed above, the combination does not render obvious the independent claim 1 and thus would not render these dependent claims obvious.


Applicants respectfully assert that the claims are in allowable form and earnestly solicit the allowance of the claims 1-10 and 22.

Appl. No. 10/526,089
Amendment dated March 10, 2008
Reply to Office action of October 10, 2007

Early and favorable consideration is respectfully requested.

Respectfully submitted,

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